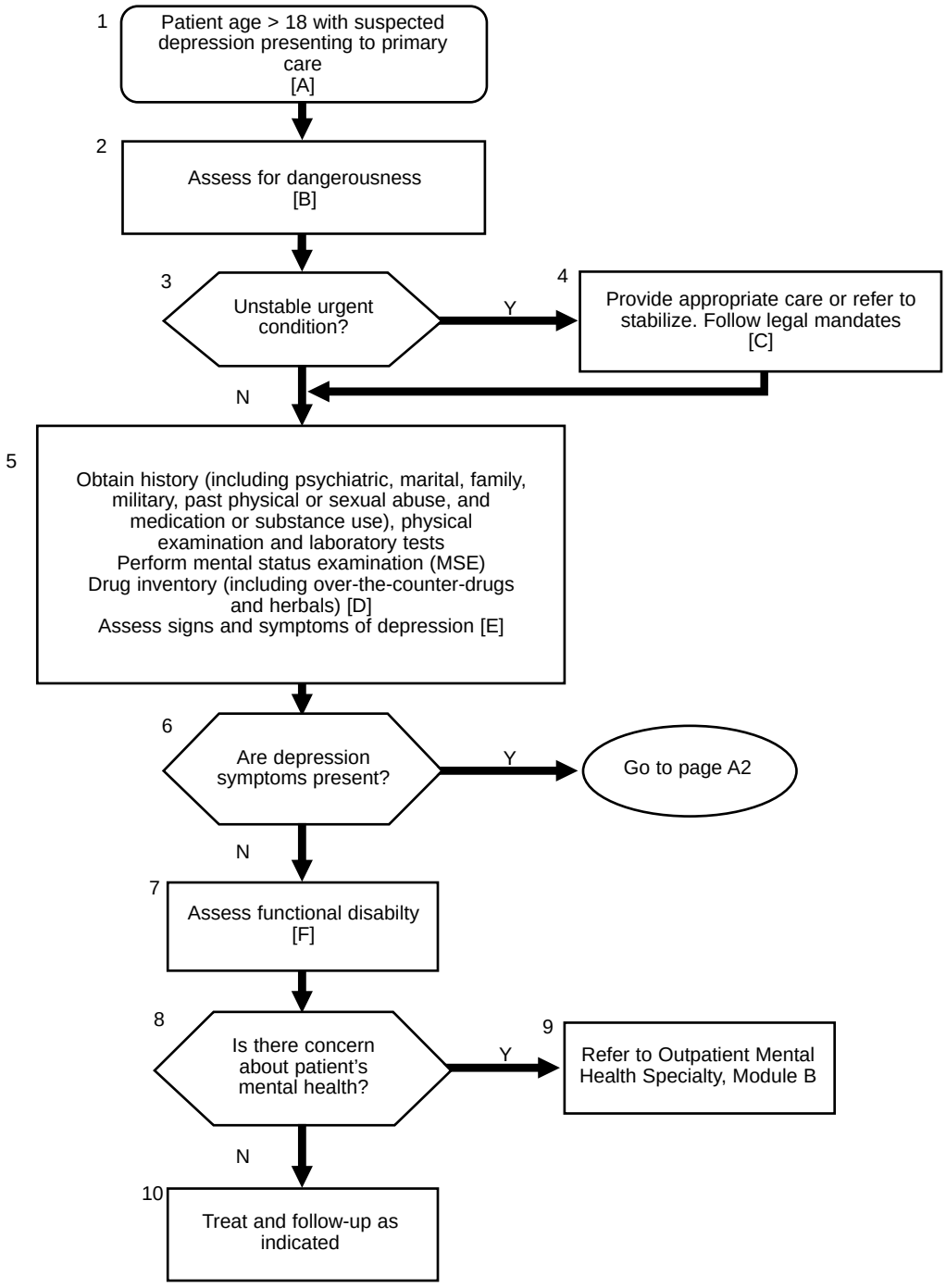
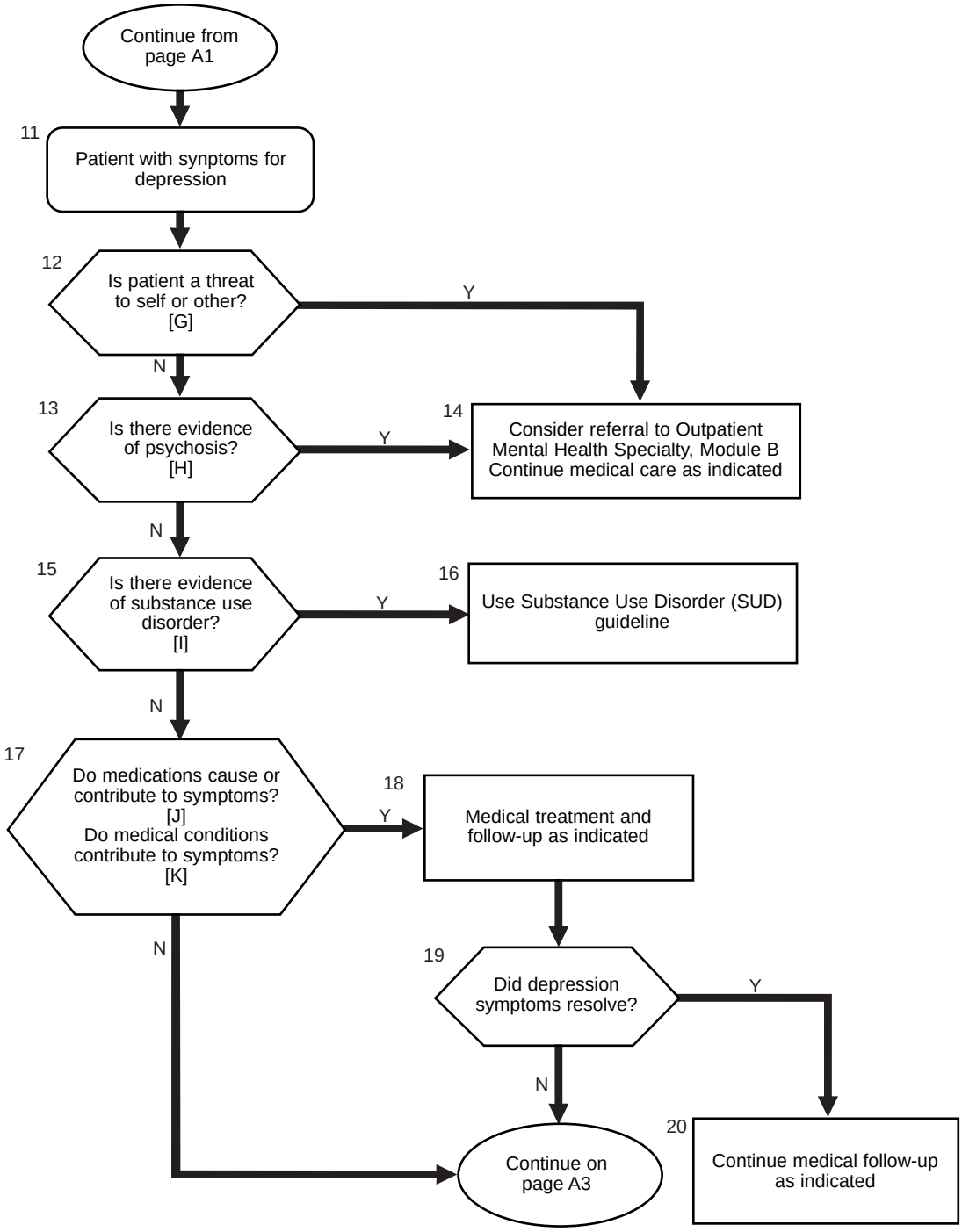
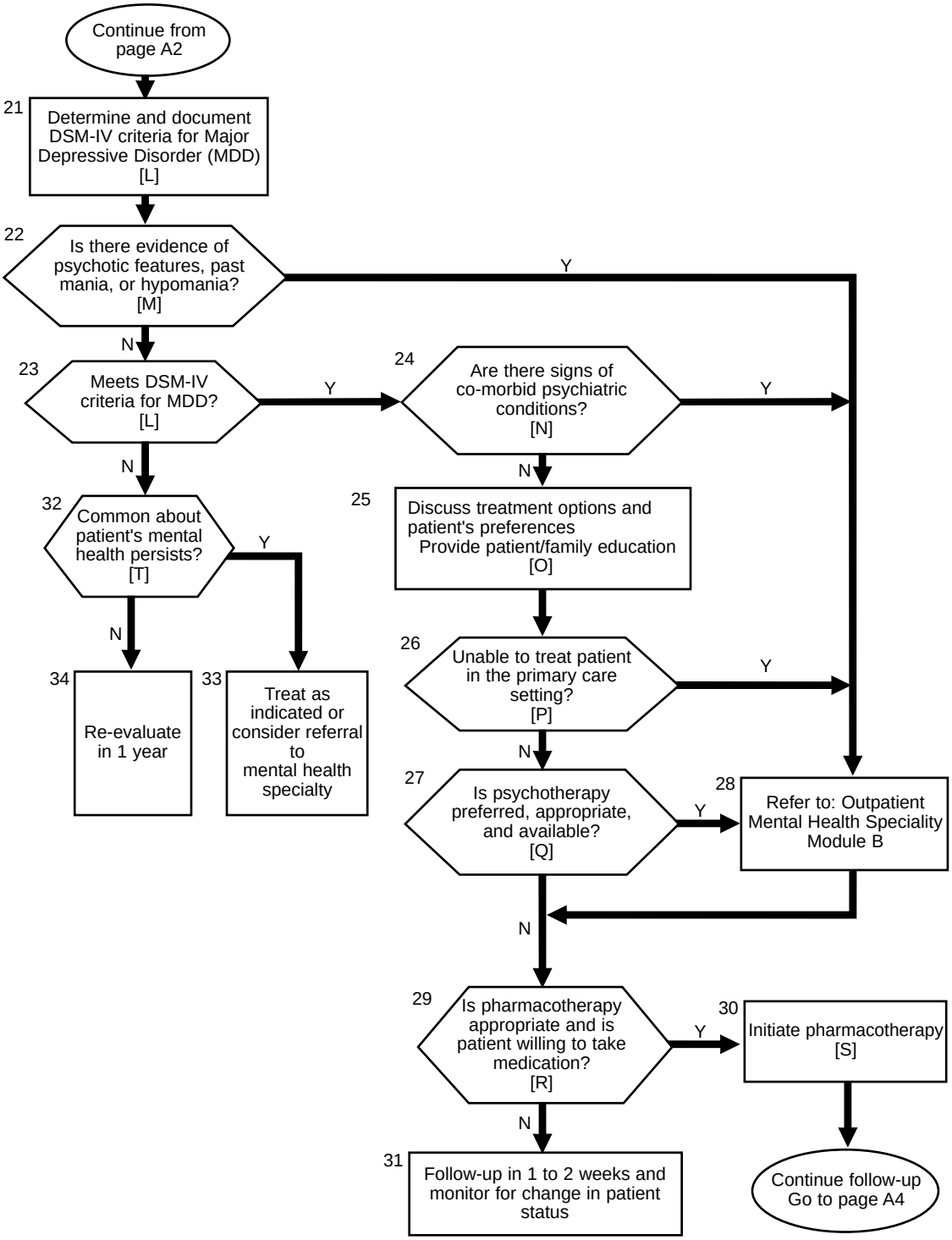
VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder in Adults: Primary Care

Guideline Summary




Continue from page A1
11
Patient with synptoms for depression
12
Is patient a threat to self or other? [G]
Y
N
13
Is there evidence of psychosis? [H]
Y
14
Consider referral to Outpatient Mental Health Specialty, Module B Continue medical care as indicated
N
15
Is there evidence of substance use disorder? [I]
Y
16
Use Substance Use Disorder (SUD) guideline
N
17
Do medications cause or contribute to symptoms? [J]
Do medical conditions contribute to symptoms? [K]
18
Y
Medical treatment and follow-up as indicated
N
19
Did depression symptoms resolve?
Y
N
20
Continue medical follow-up as indicated
Continue on page A3



VA access to full guidelines: http://www.oqp.med.va.gov/cpg/cpg.htm

DoD access to full guidelines: http://www.cs.amedd.army.mil/Qmo

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GUIDE for INTERPRETING PRIME MD
PATIENT HEALTH QUESTIONNAIRE SCORES

SCORE:	ACTION:
≤ 4	The patient may not need depression treatment.
≤ 5 – 14	Use clinical judgement about treatment, based on patient's duration of symptoms and functional impairment.
≥ 15	Warrants treatment for depression using antidepressant, psychotherapy and/or a combination treatment.

Pathobiologies Related to Depression

Pathology	Disease
Cardio/vascular	Coronary artery disease Congestive heart failure Uncontrolled hypertension Anemia Stroke Vascular Dementias
Chronic Pain Syndrome	Fibromyalgia, Reflex sympathetic dystrophy, Low back pain (LBP), Chronic pelvic pain Bone or disease related pain
Degenerative	Presbyopia Presbycusis Alzheimer's disease Parkinson's disease Huntington's disease Other Neurodegenerative diseases
Immune	HIV (both primary and infection-related) Multiple Sclerosis Systemic Lupus Erythematosis (SLE) Sarcoidosis
Infection	Systemic Inflammatory Response Syndrome (SIRS) Meningitis
Metabolic/Endocrine Conditions (include renal and pulmonary)	Malnutrition, Vitamin deficiencies Hypo/Hyperthyroidism Addison's Disease Diabetes Mellitus Hepatic disease (cirrhosis) Electrolyte disturbances Acid-base disturbances Chronic Obstructive Pulmonary Disease (COPD) or Asthma Hypoxia
Neoplasm	Of any kind, especially pancreatic or central nervous system (CNS)

MEDICATIONS THAT CAN CAUSE DEPRESSION

Evidence

QE	SR	Drug/Drug Class
I	B	Amphetamine withdrawal, Anabolic Steroids, Digitalis, Glucocorticoids
I	C	Cocaine withdrawal
II-1	C	Reserpine
II-2	A	Gonadotropin-releasing agonists, Pimozide
II-2	B	Propanolol (Beta Blockers)
II-2	C	ACE inhibitors, Antihyperlipidemics, Benzodiazepines, Cimetidine, Ranitidine, Clonidine, Cycloserine, Interferons, Levodopa, Methyldopa, Metoclopramide, Oral contraceptives, Topiramate, Verapamil (Calcium channel Blockers)

SYMPTOMS of MAJOR DEPRESSION & DYSTHYMIC D/O - "SIG-E-CAPS"

S **S**leep disorder (either increased or decreased sleep)*
I **I**nterest deficit (anhedonia)
G **G**uilt (worthlessness,* hopelessness,* regret)
E **E**nergy deficit*
C **C**oncentration deficit*
A **A**ppetite disorder (either decreased or increased)*
P **P**sychomotor retardation or agitation
S **S**uicidality

Note: To meet the diagnosis of major depression, a patient must have 5 of the symptoms plus depressed mood or anhedonia for at least 2 weeks. To meet the diagnosis dysthymic disorder, a patient must have 2 of the 6 symptoms marked with an * plus depressed mood for at least 2 years.

DEPRESSION WARNING SIGNS

- Medically unexplained physical symptoms
- Chronic debilitating medical condition
- Current substance misuse
- Medically unexplained functional status
- History or current physical or sexual abuse or emotional neglect
- Loss of significant relationship, primary support system or economic status
- Protracted care-giving role for a family member with a chronic, disabling condition
- Bereavement and widowhood
- Symptoms or signs of PTSD

INQUIRING ABOUT SUICIDAL IDEATION

- When a patient describes a depressive episode the Primary Care Provider can empathize and explore for the presence of suicidal ideation by saying:
  "You sound as if you have been feeling pretty miserable (or sad or low or dismal or despondent or down). Has life ever seemed not worth living?"
- If the patient acknowledges suicidal ideation but does not state how active the contemplation is, follow-up by asking:
  "So, you have felt life is not worth living. Have you ever thought about acting on those feelings?"
- If the patient acknowledges that s/he has, explore if the patient has a plan. If so, what is it, is it realistic, has s/he acted on it, if so, how recently?

- If the patient has made a plan, has the means or has recently acted on it, then hospitalization is needed. If the patient is in a gray area, decide how impulsive the patient is and whether a good faith agreement can be made to contact the Provider or come to an emergency care facility if suicidal ideation becomes intrusive, persistent or compelling.

DIAGNOSIS & RISK FACTORS - SECTION III, PART C - DSM-IV

Diagnosis and Risk Assessment

Review Red Flag Risk Factors. Check all that apply.

Does the patient need emergency treatment?

- ✓ Suicidal thoughts and/or plans which make you uncertain of the patient's safety.
- ✓ Assaultive/homicidal thoughts and/or plans which make you uncertain about the safety of the patient or others.
- ✓ Inability to care for self.
- ✓ Psychotic thinking.
- ✓ Mania.
- ✓ Serious mental disorder causing significant impairment of social, familial, vocational or educational functioning.
- ✓ Delirium.

If any of these conditions are present, consider referral/consultation to Behavioral Health and/or hospitalization.

Is active chemical abuse/dependency present?

If present or suspected, consider referral for a chemical dependency assessment.

Is there a history of non-compliance with or abuse of psychopharmacological medication?

If present or suspected, refer to Behavioral Health.

Is there a strong suggestion of a personality disorder?

If present or suspected, refer to Behavioral Health.

TREATMENT of DEPRESSION

Pharmacologic Treatment of Depression

General Principles of Pharmacotherapy

- No agent has been proven to be superior to another in efficacy or time to response.
- Use what has worked for the patient in the past.
- The most common cause of treatment failure is an inadequate medication trial.
- If no response at 4-6 weeks, consider switching, combining or augmenting the pharmacotherapy.
- SSRIs are agents of first choice due to ease of use, more tolerable side effects and safety in overdose.
- Counsel pregnant women and those considering pregnancy. The potential risks and benefits of pharmacotherapy must be weighed.

Managing Medication Side Effects

- Insomnia - Consider Diphenhydramine at HS or a brief trial of a short-acting non-addictive BZ receptor-binding agent, then reassess.
- Akathisia - Associated with newer antidepressants. Consider adding a small dose of clonazepam (0.5 mg q HS) or propanolol (10-20 mg bid/tid).
- Sexual dysfunction - Common with all SSRIs and others. Bupropion is least likely to

General Principles of Psychotherapy

- Evidence-based psychotherapies are as effective as antidepressant medication for most patients and may be considered as first line treatment in most cases.
- Evidence-based psychotherapies for depression are all brief, focused on current concerns, and help the patient learn new skills or alter patterns of behavior.
- Patients must be active psychotherapy participants who attend sessions consistently and follow

through on actionplans between sessions.

- If patient is not engaged in therapy after 6 weeks or is worse, consider antidepressant medication as addition or alternative. If patient is not improved after 12 weeks, medication should become a component of treatment.
- Combination of psychotherapy and medication should be tried for patients who have not responded to either approach alone during the current episode or who have responded well to combination therapy in prior episodes.

Types of Short-Term Psychotherapy

- Interpersonal Psychotherapy focuses on clarification and resolution of difficulties in relationships, exploring losses, role disputes and transitions, and social skills deficits.
- Behavior Therapy addresses behavioral activation, self-control, and social skills training.
- Cognitive Therapy explores self-destructive cognition and aims at modification of negatively biased thoughts.
- Cognitive-Behavioral Therapy combines elements of cognitive and behavioral approaches, emphasizing both behavioral activation and changes in negatively biased patterns of cognition. This approach has the most research supporting its effectiveness for immediate gains during current episode and long term benefit in preventing future episodes.
- Short-term Psychodynamic Psychotherapy maintains focus on present difficulties but recognizes past as influencing present issues. Emphasizes insight into defenses and analysis of transference and resistance. Less evidence regarding this approach is available
- Marital Therapy focuses on spousal interactions and appears to be effective for depressed women in marital relationships with significant discord, although less evidence regarding this approach is available.

Ongoing Clinical Assessment

- Initially, see patients at least every 1-2 weeks for 4-6 weeks. Assess treatment compliance and response to intervention. Evaluate suicidal tendencies, answer questions, rule out comorbid disorders, and/or refer for additional therapy component.
- If on medication, assess/ reassure patient regarding side effects and adjust medication as needed. When therapeutic medication response is reached, continue same dosage for 4-9 months. Maintain office visits or telephone contact monthly for 6 months thereafter. Lifetime medication maintenance is recommended for patients with 3 or more episodes of major depression.
- If in psychotherapy, monitor response and adapt therapy as needed. When symptoms have remitted, develop a maintenance plan to prevent reoccurrence. Consider occasional booster sessions over the next six months to 1 year.

DSM-IV - COMMON MOOD DISORDERS (not inclusive)

D E P R E S S I V E D I S O R D E R S

DSM-IV Code	DIAGNOSIS	DESCRIPTION / CRITERIA
296.2x	**Major Depressive Disorder, Single Episode**	A. Five (or more) of the following symptoms have been present during the same two week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. **Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.** (1) depressed mood most of the day, nearly every day, as indicated by either subjective report or observation made by others (2) markedly diminished interest or pleasure in all, or almost all activities most of the day, nearly every day, as indicated by either subjective account or observation made by others

DSM-IV Code	DIAGNOSIS	DESCRIPTION / CRITERIA
296.2x	**Major Depressive Disorder, Single Episode**	(3) significant weight loss when not dieting or weight gain (a change of more than 5% of body weight in a month), or decrease/increase in appetite nearly every day (4) insomnia or hypersomnia nearly every day (5) psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down) (6) fatigue or loss of energy nearly every day (7) feelings of worthlessness, or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick) (8) diminished ability to think or concentrate, or indecisiveness, nearly every day, (either by subjective account or as observed by others) (9) recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide B. The symptoms do not meet criteria for a Mixed Episode. C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. D. The symptoms are not due to the direct physiological effects of a substance (drug of abuse/medication) or a general medical condition (hypothyroidism). E. The symptoms are not better accounted for by Bereavement.
296.3x	**Major Depressive Disorder, Recurrent**	Any condition classifiable as **296.2** that is recurrent. See above description.
300.4	**Dysthymic Disorder**	A. Depressed mood for most of the day, for more days than not, as indicated by either subjective account or observation by others, for at least two years. B. Presence, while depressed of two or more of the following: (1) poor appetite or overeating (2) insomnia or hypersomnia (3) low energy or fatigue (4) low self-esteem (5) poor concentration or difficulty making decisions (6) feelings of hopelessness C. During the two year period the person has never been without the symptoms of A or B for more than 2 months at a time. D. No Major Depressive Episode has been present during the first two years of the disturbance; the disturbance is not better accounted for by chronic Major Depressive Disorder or Major Depressive Disorder, in Partial Remission. E. There has never been a Manic Episode, a Mixed Episode or a Hypomanic Episode and criteria has never been met for Cyclothymic D/O. F. Disturbance does not occur exclusively during course of a chronic Psychotic D/O. G. The symptoms are not due to the direct physiological effects of a substance (drug of abuse/medication) or a general medical condition (hypothyroidism). H. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

DSM-IV 5th Digit Subclassification Codes: Add to 296.0 to 296.6 where the "x" is located

0 Unspecified	2 Moderate	4 Severe, with Psychotic Behavior	6 Full Remission
1 Mild	3 Severe, No Psychotic Behavior	5 In Partial or Unspecified Remission	

ANTIDEPRESSANT MEDICATION TABLE

Refer to pharmaceutical manufacturer's literature for full prescribing information

SEROTONIN SELECTIVE REUPTAKE INHIBITORS (SSRIs)

GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Citalopram	Celexa	20 mg	60 mg	Reduce dose for the elderly & those with renal or hepatic failure	No serious systemic toxicity even after substantial overdose. Drug interactions may include tricyclic antidepressants, carbamazepine & warfarin.	Nausea, insomnia, sedation, headache, fatigue dizziness, sexual dysfunction anorexia, weight loss, sweating, GI distress, tremor, restlessness, agitation, anxiety.	Response rate = 2 - 4 wks	AM daily dosing. Can be started at an effective dose immediately.
Fluoxetine	Prozac	20 mg	80 mg					
Paroxetine	Paxil	20 mg	50 mg					
Sertraline	Zoloft	50 mg	200 mg					

First Line Antidepressant Medication
Drugs of this class differ substantially in safety, tolerability and simplicity when used in patients on other medications. Can work in TCA nonresponders. Useful in several anxiety disorders. Taper gradually when discontinuing these medications. Fluoxetine has the longer half-life.

SEROTONIN and NOREPHINEPHRINE REUPTAKE INHIBITORS (SNRIs)

GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Venlafaxine IR	Effexor IR	75 mg	375 mg	Information Not Available	No serious systemic toxicity. Downtaper slowly to prevent clinically significant withdrawal syndrome. Few drug interactions.	Comparable to SSRIs at low dose. Nausea, dry mouth, insomnia, somnolence, dizziness, anxiety, abnormal ejaculation, headache, asthenia, sweating.	Response rate = 2 - 4 wks (4 - 7 days at ~300 mg/day)	BID or TID dosing with IR. Daily dosing with XR. Can be started at an effective dose (75 mg) immediately.
Venlafaxine XR	Effexor XR	75 mg	375 mg					

Dual action drug that predominantly acts like a Serotonin Selective Reuptake inhibitor at low doses and adds the effect of an Norepinephrine Selective Reuptake Inhibitor at high doses. Possible efficacy in cases not responsive to TCAs or SSRIs. Taper dose prior to discontinuation.

SEROTONIN (5-H2A) RECEPTOR ANTAGONIST and WEAK SEROTONIN REUPTAKE INHIBITORS

GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Nefazodone	Serzone	200 mg	600 mg	Reduce dose for the elderly & those with renal or hepatic failure	No serious systemic toxicity from OD. Can interact with agents that decrease arousal/impair cognitive performance and interact with adrenergic agents that regulate blood pressure.	Somnolence dizziness, fatigue, dry mouth, nausea, headache, constipation, impaired vision. Unlikely to cause sexual dysfunction.	Response rate = 2 - 4 wks	BID dosing. Requires dose titration.
Trazodone	Desyrel	150 mg	600 mg					

Corrects sleep disturbance and reduces anxiety in about one week.

DOPAMINE and NOREPINEPHRINE REUPTAKE INHIBITORS (DNRIs)

GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Bupropion - IR	Wellbutrin - IR	200 mg	450 mg	Reduce dose for the elderly & those with renal or hepatic failure	Seizure risk at doses higher than max. Drug/drug interactions uncommon.	Rarely causes sexual dysfunction.	Response rate = 2 - 4 wks	BID / TID dosing. Requires dose titration.
Bupropion - SR	Wellbutrin - SR	150 mg	400 mg					

Least likely antidepressant to result in a pt becoming manic. Do not use if there is a history of seizure disorder, head trauma, bulimia or anorexia. Can work in TCA nonresponders.

TRICYCLIC ANTIDEPRESSANTS (TCAs) – Mainly Serotonin Reuptake Inhibitors

GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Amitriptyline *	Elavil, Endep *	50 - 100 mg	300 mg	Reduce dose for those with renal or hepatic failure	Serious toxicity can result from OD. Slow system clearance. Can cause multiple drug/drug interactions.	Sedation, increased anticholinergic effects, orthostatic hypotension, cardiac conduction disturbances, arrhythmia & wt gain, dizziness, sexual dysfunction.	Response rate = 2 - 4 wks Therapeutic Levels: Imipramine 200-350 ng/mL	Can be given QD. Monitor serum level after one week of treatment.
Imipramine *	Tofranil *	75 mg	300 mg					
Doxepin *	Sinequan *	75 mg	300 mg					

These antidepressants are not recommended for use in the elderly.
Highest response rates. TATCAs useful in chronic pain, migraine headaches & insomnia.

* Tertiary Amine Tricyclic Antidepressants (TATCAs).

TRICYCLIC ANTIDEPRESSANTS (TCAs) – Mainly Norepinephrine Reuptake Inhibitors

GENERIC	BRAND NAME	ADULT STARTING DOSE	MAX	EXCEPTION	SAFETY MARGIN	TOLERABILITY	EFFICACY	SIMPLICITY
Desipramine *	Norpramin *	75 - 200 mg	300 mg	Reduce dose for the elderly & those with renal or hepatic failure	Serious toxicity can result from OD. Reserve Maprotiline as a second-line agent due to risk of seizures at therapeutic & nontherapeutic doses.	Generally Good	Response rate = 2 - 4 wks Therapeutic Levels: Desipramine 125-300 ng/mL Nortriptyline 50-150 ng/mL	Can be given QD. Can start effective dose immediately. Monitor serum level after one week of treatment.
Nortriptyline	Aventyl/Pamelor	50 mg	150 mg					

Consider Desipramine or Nortriptyline first in the elderly if TCAs are necessary.

* Secondary Amine Tricyclic Antidepressants (SATCAs)

CRITERIA #5 – EDUCATION/INSTRUCTION

- **What is Major Depression?** - An illness that may be associated with biochemical changes in brain function. More than just a feeling of sadness, it affects day-to-day thoughts, feelings, actions, and physical well-being.
- **Myths** - Major depression is not a trivial disorder, will usually not go away on its own and is not the result of personal weakness, laziness or lack of will power.
- **Incidence** - Depression is a common illness affecting one out of every 20 people sometime in their lifetime.
- **Risk Factors** - Females, people with a first-degree relative with depression, a history of drug or alcohol misuse or a history of anxiety or eating disorders have an increased chance of having depression.
- **Treatment Response** - Depression responds well to treatment. People do get better.
- **Treatment Options** - Include antidepressant medication, psychotherapy, or a combination of the two. Sometimes treatment is done in primary care or family practice and sometimes in a mental health clinic, depending on your individual circumstances.
- **Outpatient vs Inpatient Care** - Most people with depression are successfully treated as outpatients. Inpatient hospitalization is generally reserved for patients with very severe symptoms.
- **Consultation/Referral** - Frequently a treatment team approach is used. A combination of treatments might work best, especially if the depression is severe or lasts a long time or the first treatment did not work well.
- **Medications** - Antidepressant medication takes a few weeks to get the full effect. It won't work if you don't take it consistently. Don't worry it's safe and not addicting.
- **Medication Side Effects** - Discuss side effects or other problems with your provider. Most problems can be resolved.
- **Treatment Takes Time** - Be consistent. Stick to your treatment plan. Follow-up with all scheduled appointments. Follow through on treatment steps or homework assignments. Remember, medication must be taken as directed, including dosage, frequency and length of time prescribed.
- **Don't** - Drink alcohol, self-medicate, or blame yourself. Talk with your provider before making major life decisions or changes during treatment.
- **Do** - Get plenty of rest, exercise, eat regularly, socialize.
- **Suicide** - Thoughts of death often accompany depression. Discuss these thoughts with your provider. If your provider is not available, seek immediate emergency care or tell a trusted friend or relative who can help you get professional help right away.
- **Communication** - Work with your provider. Discuss treatment options. Ask questions about treatment and talk about any concerns you may have. Discuss with your provider your feelings, activity, sleep and eating patterns, as well as unusual symptoms or physical problems.
- **Recurrence** - Depression may be recurrent. Maintenance antidepressants or booster therapy sessions may be needed for long-term health.

MONITORING & FOLLOW-UP DOCUMENTATION

Monitor response to therapy, treatment adherence, medication side effects, etc. every 1-2 weeks. Assess response at 4-6 weeks and adjust therapy as indicated. Reassess response at 12 weeks. Consider consultation/referral for an incomplete response.